

**2016 Children's Safe Products - Reporting Rule update**  
**Draft Chemical Evaluation**

**CAS** 115-86-6

**Substance Name** Triphenyl phosphate (**TPP** or TPHP)

**Toxicity**

EPA classified TPP as a high hazard for toxicity from repeated exposures [1]. Decreased body weight gain in adult rats was the most sensitive endpoint reported following repeated oral exposure; the lowest-observed-adverse-effect-level (LOAEL) was 161 mg/kg-day. At higher doses, reproductive and fetal effects were observed [1]. TPP appears to be active in endocrine tissues. In a recently published study, mice exposed to 300 mg/kg-day TPP orally for 35 days had decreased testes weight, histopathological damage, decreased testicular testosterone levels, decreased expression of genes related to testosterone synthesis, and signs of oxidative stress in the liver [2]. *In vitro* testing shows that TPP is a moderate androgen-receptor binder and can inhibit receptor function (testosterone-induced androgen-receptor-dependent activity) [1]. TPP and its hydroxylated metabolites acted as estrogen receptor agonists in other *in vitro* studies [3, 4]. Only limited human evidence of endocrine disruption is available. A study in Boston, Massachusetts reported that men living in homes with higher TPP in house dust had decreased sperm counts and altered hormone (prolactin) levels [5].

There is also emerging evidence that TPP may cause long-lasting metabolic disruption in rats exposed during fetal and nursing periods [6, 7]. Green et al., 2016 showed that developmental exposure to TPP alone, caused accelerated onset of type 2 diabetes in a rat diabetes model and increased body fat later in life [7]. The very low dose used in this study (17 µg/rat-day; <0.5 mg/kg-day) was not associated with overt toxicity or weight change in treated dams or offspring at birth. It was equivalent to the dose of TPP present in a study by Patisaul et al., 2013, that observed metabolic disruption in offspring following developmental exposure to 1 mg/rat-day of Firemaster® 550 [6]. These study results suggest a high hazard for developmental toxicity.

Investigators at the National Toxicology Program used cell-based *in vitro* assays and assays in rapidly developing whole organisms (in this case, the nematode *C. elegans*) to screen for potential developmental toxicity and neurotoxicity of a number of phosphate flame retardants [8, 9]. TPP had a more potent impact on larval development than PBDE<sup>1</sup> flame retardants and was a relatively strong inhibitor of mitochondrial activity in *in vitro* testing [9].

**Exposure**

TPP is a plasticizing flame retardant in PVC. It is also used as a flame retardant in other polymers, textiles, polyurethane foam, electronic circuit boards, photographic films, and building materials. [10, 11]. It is a component of Firemaster® 550 used in polyurethane foams and has been detected in baby products [11, 12] other children's products, carpet pads, and plastic parts of LCD monitors [13]. TPP is an additive flame retardant and migrates from computer monitors and TV sets [11]. TPP is also used as a plasticizer and may be in clothing, textiles, cosmetics, and personal care products [14]. It is listed as an

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<sup>1</sup> Pbde - polybrominated diphenyl ether

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ingredient in nail polish and a recent biomonitoring study showed short-term spikes in exposure following application of nail polish [15]. U.S. national production volume was reported to be 10,796,422 million pounds per year in 2012 [16].

Because of its physical properties, TPP that escapes from consumer products, either by emission or abrasion, is likely to end up in indoor dust. TPP was detected at high levels in indoor dust in studies of homes in North Carolina, Boston, California, and Canada [17-20]. Maximum detected level was 1,800 µg/g dust. It has also been detected in U.S. office and vehicle dust [21]. TPP has also been measured in the indoor air of homes and public buildings in a number of countries. Maximum level reported was 100 ng/m<sup>3</sup> [11].

Diphenyl phosphate (DPHP), a metabolite of TPP, has been found in urine at high frequency (>90%) in North American biomonitoring studies including Boston adults [22], New Jersey mothers and toddlers [23], California mothers and their children aged 2-70 months [24], and North Carolina babies [25]. Levels measured in children were higher than their mothers [23, 24, 26] and were higher in children with more reported hand-to-mouth behaviors [23, 24]. Mean and median levels of DPHP in urine reported across these studies have been less than 3.2 ng/mL with a maximum reported level of 140 ng/mL. TPP has been measured up to 140 ng/g lipid in human breast milk in Asian and Swedish studies [27, 28]. TPP was detected in 98% of hair samples and 74% of finger and toenail samples in a population of young adults in Indiana [29].

TPP appears to be ubiquitous in the environment and has been detected in drinking water, river water, seawater, rainwater, snow, wastewater effluent, ambient air, and indoor air [1, 11, 18, 30-33].

### References

1. EPA, *Flame Retardants Used in Flexible Polyurethane Foam: An Alternatives Assessment Update*. 2015, U.S. Environmental Protection Agency.
2. Chen, G., et al., *Exposure of male mice to two kinds of organophosphate flame retardants (OPFRs) induced oxidative stress and endocrine disruption*. *Environ Toxicol Pharmacol*, 2015. **40**(1): p. 310-8.
3. Hiroyuki Kojima, S.T., Nele Van den Eede, Adrian Covaci, *Effects of primary metabolites of organophosphate flame retardants on transcriptional activity via human nuclear receptors*. *Toxicology Letters*, 2016. **245**: p. 31-39.
4. Boris V. Krivoshiev, F.D., Adrian Covaci, Ronny Blust, Steven J. Husson, *Assessing in-vitro estrogenic effects of currently-used flame retardants*. *Toxicology in Vitro*, 2016. **33**: p. 153-162.
5. Meeker, J.D. and H.M. Stapleton, *House dust concentrations of organophosphate flame retardants in relation to hormone levels and semen quality parameters*. *Environ Health Perspect*, 2010. **118**(3): p. 318-23.
6. Patisaul, H.B., et al., *Accumulation and endocrine disrupting effects of the flame retardant mixture Firemaster(R) 550 in rats: an exploratory assessment*. *J Biochem Mol Toxicol*, 2013. **27**(2): p. 124-36.
7. Green, A.J., et al., *Perinatal triphenyl phosphate exposure accelerates type 2 diabetes onset and increases adipose accumulation in UCD-type 2 diabetes mellitus rats*. *Reprod Toxicol*. 2016 Jul 12. doi: 10.1016/j.reprotox.2016.07.009. [Epub ahead of print].

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8. Behl, M., et al., *Use of alternative assays to identify and prioritize organophosphorus flame retardants for potential developmental and neurotoxicity*. *Neurotoxicology and Teratology* **52** (2015) 181–193.
9. Behl, M., et al., *Comparative Toxicity of Organophosphate Flame Retardants and Polybrominated Diphenyl Ethers to Caenorhabditis elegans*. *Toxicol Sci.* 2016 Aug 26. pii: kfw162 [Epub ahead of print].
10. Brooke, D., Crookes, M, Quaterman, P, Burns, J, *Environmental Risk Evaluation Report: Triphenyl Phosphate (CAS no. 115-86-6)*. 2009, Environment Agency, Bristol, UK: United Kingdom. p. 140.
11. Toxicology Excellence for Risk Assessment (TERA), *Environmental Concentrations and Consumer Exposure Data for Selected Flame Retardants (TDCPP, TCPP, TEP, TPP)*. June 1, 2015: Consumer Product Safety Commission contract Number CPSC-D-12-0001.
12. Stapleton, H.M., et al., *Identification of flame retardants in polyurethane foam collected from baby products*. *Environ Sci Technol*, 2011. **45**(12): p. 5323-31.
13. Ecology, *Flame Retardants in General Consumer and Children's Products*. Washington State Department of Ecology, June 2014, Publication No. 14-04-021.
14. ECHA, *Brief Profiles: Triphenyl Phosphate* [accessed September 2016]. Available at <https://echa.europa.eu/information-on-chemicals>.
15. Emma Mendelsohn, A.H., Kate Hoffman, Craig M. Butt, Amelia Lorenzo, and T.F.W. Johanna Congleton, Heather M. Stapleton, *Nail polish as a source of exposure to triphenyl phosphate*. *Environment International*, 2016. **86**: p. 45-51.
16. EPA. *Chemical Data Access Tool (CDAT) - Chemical Data Reporting (CDR) information on the production and use of chemicals manufactured or imported into the United States*. 2012 10/15/2015 10/30/2015]; Available from: [http://java.epa.gov/oppt\\_chemical\\_search/](http://java.epa.gov/oppt_chemical_search/).
17. Hoffman, K., et al., *Monitoring indoor exposure to organophosphate flame retardants: hand wipes and house dust*. *Environ Health Perspect*, 2015. **123**(2): p. 160-5.
18. Stapleton, H.M., et al., *Detection of Organophosphate Flame Retardants in Furniture Foam and U.S. House Dust*. *Environmental Science & Technology*, 2009. **43**(19): p. 7490-7495.
19. Dodson, R.E., et al., *After the PBDE phase-out: a broad suite of flame retardants in repeat house dust samples from California*. *Environ Sci Technol*, 2012. **46**(24): p. 13056-66.
20. Fan, X., et al., *Simultaneous determination of thirteen organophosphate esters in settled indoor house dust and a comparison between two sampling techniques*. *Sci Total Environ*, 2014. **491-492**: p. 80-6.
21. Springer, C., et al., *Rodent thyroid, liver, and fetal testis toxicity of the monoester metabolite of bis-(2-ethylhexyl) tetrabromophthalate (tbph), a novel brominated flame retardant present in indoor dust*. *Environ Health Perspect*, 2012. **120**(12): p. 1711-9.
22. Meeker, J.D., et al., *Urinary metabolites of organophosphate flame retardants: temporal variability and correlations with house dust concentrations*. *Environ Health Perspect*, 2013. **121**(5): p. 580-5.
23. Butt, C.M., et al., *Metabolites of organophosphate flame retardants and 2-ethylhexyl tetrabromobenzoate in urine from paired mothers and toddlers*. *Environ Sci Technol*, 2014. **48**(17): p. 10432-8.
24. Butt, C.H., K; Chen, A; Lorenzo, A; Congleton, J; Stapleton, HM, *Regional comparison of organophosphate flame retardant (PFR) urinary metabolites and tetrabromobenzoic acid (TBBA) in mother-toddler pairs from California and New Jersey*. *Environment International*, 2016. **94**: p. 627-34.
25. Hoffman, K., et al., *High Exposure to Organophosphate Flame Retardants in Infants: Associations with Baby Products*. *Environ Sci Technol*, 2015. **49** (24), pp 14554–14559.

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26. Cequier, E., et al., *Human exposure pathways to organophosphate triesters - a biomonitoring study of mother-child pairs*. Environ Int, 2015. **75**: p. 159-65.
27. Kim, J.W., et al., *Organophosphorus flame retardants (PFRs) in human breast milk from several Asian countries*. Chemosphere, 2014. **116**: p. 91-7.
28. Sundkvist, A.M., U. Olofsson, and P. Haglund, *Organophosphorus flame retardants and plasticizers in marine and fresh water biota and in human milk*. J Environ Monit, 2010. **12**(4): p. 943-51.
29. Liang-Ying Liu, K.H., Ronald A. Hites, and Amina Salamova, *Hair and Nails as Noninvasive Biomarkers of Human Exposure to Brominated and Organophosphate Flame Retardants*. Environ. Sci. Technol. 2016, 2016. **50**: p. 3065–3073.
30. van der Veen, I. and J. de Boer, *Phosphorus flame retardants: properties, production, environmental occurrence, toxicity and analysis*. Chemosphere, 2012. **88**(10): p. 1119-53.
31. Salamova, A., et al., *High Levels of Organophosphate Flame Retardants in the Great Lakes Atmosphere*. Environmental Science & Technology Letters, 2014. **1**(1): p. 8-14.
32. Cao, S., et al., *Levels and distributions of organophosphate flame retardants and plasticizers in sediment from Taihu Lake, China*. Environ Toxicol Chem, 2012. **31**(7): p. 1478-84.
33. Stiles, R., et al., *Measurement of drinking water contaminants by solid phase microextraction initially quantified in source water samples by the USGS*. Environ Sci Technol, 2008. **42**(8): p. 2976-81.